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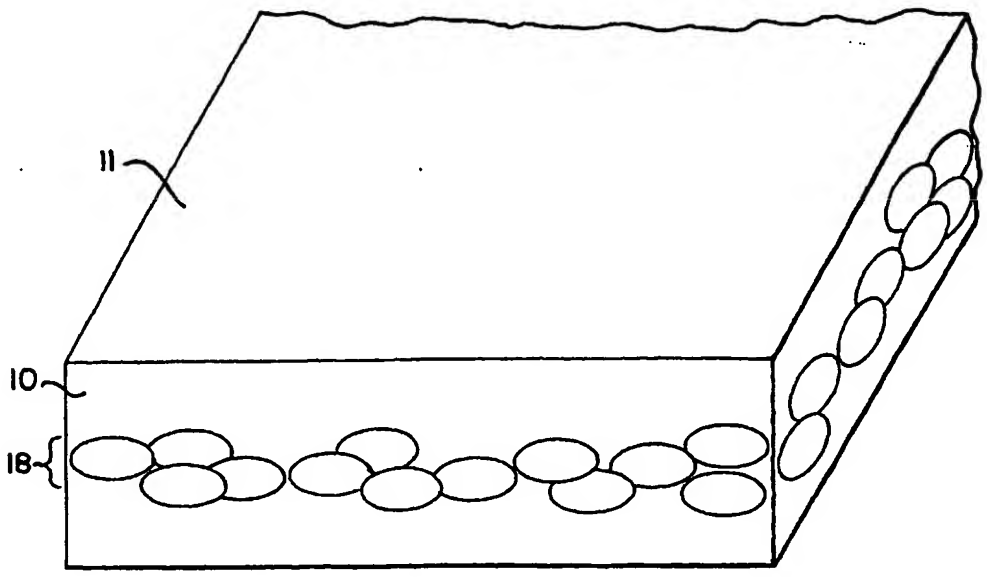

(57) Abstract: Microporous membranes (10) comprising polyvinylidene difluoride and methods for making such membranes are disclosed. The membranes (10), which are not crosslinked and are not contacted with a strong alkali solution during manufacture, are wettable by aqueous solution even after repeated wetting and drying. The membrane includes a support (18) and surfaces (11) treated with a hydrophilic coating. Separately, such membranes are also useful in apparatus (60) for separating a biological fluid into two or more components.

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POLYVINYLIDENE DIFLUORIDE MEMBRANES AND METHODS FOR MAKING SUCH MEMBRANES

The present invention relates generally to microporous, polyvinylidene difluoride (PVDF) membranes and to methods for making such membranes. More particularly, the present invention is directed to PVDF membranes (and the methods for making such membranes) that are hydrophilic and that retain their hydrophilic properties even after repeated wetting and drying.

BACKGROUND

The use of PVDF membranes for liquid filtration is well known. However, PVDF is inherently hydrophobic (lacking affinity for water). Therefore, to use a PVDF membrane to filter aqueous fluid, the membrane must first be made hydrophilic (i.e., readily wet by water). To render it hydrophilic, PVDF is typically treated with a wetting agent or surfactant.

One drawback with treated PVDF membranes is the possibility of extraction or leaching of the agent or surfactant from the membrane and into the filtrate during membrane use. This may be of particular, although not exclusive, concern where the PVDF membrane is used in the processing of a biological fluid (such as blood) which is intended for administration to a human. Extraction of the surfactant or wetting agent may also result in the loss of hydrophilicity and diminishes the efficiency or usefulness of the membrane as a filter for filtering aqueous solutions. Loss of hydrophilicity may also prevent reuse of the membrane. Although reuse may not be much of a concern where the membrane is part of a

disposable fluid processing device (and only intended for one-time use), such as in filters used in medical care or treatment, a reusable membrane may be desirable in other settings.

Methods have been developed for treating PVDF membranes to ensure that the surfactant or the wetting agent remains on the surface of the membrane and/or is not substantially extracted during use. For example, U.S. Patent No. 4,618,533 discloses a composite PVDF membrane. The PVDF membrane is made, in part, by placing the membrane in a reagent bath that includes a free radical polymerizable monomer, a polymerization initiator and a cross-linking agent. A polymerization reaction is carried out which results in a porous membrane having a permanent hydrophilic coating grafted and/or deposited thereon.

U.S. Patent No. 5,032,331 discloses a process of impregnating the pores of a hydrophobic PVDF membrane with a solution that renders the pores of the PVDF membrane hydrophilic. After the impregnation step, the PVDF membrane is subjected to a chemical treatment in a strong alkali solution containing an oxidizing agent. According to the patent, the membrane, thus treated, exhibits "semi-permanent hydrophilicity and could be dried and used cyclically."

As seen from the above, existing methods of making hydrophilic and rewettable PVDF membranes typically involve additional chemical and/or cross-linking steps. Thus, it would be desirable to provide a porous, hydrophilic PVDF membrane (and a method for making it) that does not require such steps, is repeatedly wettable and does not result in a high level of extractables.

SUMMARY

The present invention is generally embodied in a rewettable, porous, hydrophilic PVDF membrane and in a method for making such a membrane. In accordance with the first-mentioned aspect of the present invention, a microporous membrane is provided that includes (1) a porous layer of polyvinylidene difluoride (PVDF) and (2) a polyvinyl alcohol coating on the PVDF layer, sufficient to render it hydrophilic. The membrane is rewettable by an aqueous liquid after drying and is not cross-linked or contacted with a strong alkali solution. Yet it remains substantially rewettable, even after repeated wetting and drying.

In one aspect of the present invention, such a membrane remains hydrophilic even after exposure or contact with an aqueous liquid as hot as 40°C and conceivably as hot as approximately 100°C.

In one embodiment, the polyvinyl alcohol coating solution comprises approximately 1-2%, by weight, of polyvinyl alcohol dissolved in a solution of water and alcohol, such as isopropyl alcohol. The solution may include 20-80% water and 20-80% isopropyl alcohol, by weight. Further, the polyvinyl alcohol is derived from polyvinyl acetate having a degree of saponification between about 80-100%.

In another aspect, the present invention is directed to a method for making a microporous, non-crosslinked, rewettable, hydrophilic PVDF membrane. The method includes providing a porous, dry, hydrophobic PVDF membrane and contacting the membrane with a coating solution. The coating solution is made from polyvinyl alcohol dissolved in a solution of water and alcohol.

In one embodiment, the coating solution is provided by dissolving the polyvinyl alcohol in a solution of

water and alcohol, such as isopropyl alcohol. The solution may include 20-80% water and 20-80% isopropyl alcohol, by weight. The membrane may be coated by immersing the PVDF membrane in a bath of the polyvinyl alcohol coating solution.

In another aspect, the present invention is directed to an apparatus for separating a biological fluid into two or more components. The apparatus includes a housing comprising an interior wall defining a fluid chamber, a fluid inlet and at least one fluid outlet which communicate with the chamber. The apparatus also includes a rotor within the chamber and a microporous membrane disposed on either one of the interior wall or the rotor. The membrane is made of a porous layer of polyvinylidine difluoride and a polyvinyl alcohol coating thereon sufficient to render the polyvinylidene difluoride layer hydrophilic.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a cross-sectional view of a membrane embodying the present invention without an internal support;

Figure 1A is a cross sectional view of another membrane embodying the present invention with an internal support;

Figure 2 is a diagram showing the method of making PVDF membranes in accordance with the present invention; and

Figure 3 is a perspective view of a separation device incorporating a PVDF membrane embodying the present invention, with a portion of the device broken away to show the device interior.

DETAILED DESCRIPTION

Membranes of the present invention may be flat sheet, porous membranes. One embodiment of a membrane 10 embodying the present invention is generally depicted in Fig. 1. Membrane 10 typically includes one or more layers of a polymeric material that includes polyvinylidene difluoride (PVDF). The layers may be made entirely of PVDF or may be made of a blend of PVDF and other suitable polymers and copolymers. Thus, as used herein, the term "PVDF membrane" or "PVDF layer" encompasses membranes or layers made entirely of PVDF and/or blends of PVDF with other polymers and/or copolymers. The surfaces 11 of PVDF membrane are typically treated with a hydrophilic coating. In one specific and preferred embodiment, PVDF membranes are coated with a wetting agent such as polyvinyl alcohol.

Alternatively, and more preferably, as shown in Fig. 1A, the membrane 10 may be used in association with an internal support 18, typically made of a fibrous, porous polymeric material such as polyester mesh, onto which one or more layers of PVDF is applied to form the PVDF membrane.

In one example, membranes (with the internal support) may have a thickness of approximately 4-7 mils or approximately .004-.007 inches. Typically, the membranes are substantially isotropic but may also be anisotropic (i.e., where the pore size changes from one surface of the membrane to the other). Membranes made in accordance with the present invention may be "microporous" membranes, having a nominal pore size of less than about 100 microns and typically between approximately 0.01-10 microns. In addition, membranes made in accordance with the present invention may be "ultrafiltration" membranes, having a nominal pore size

of less than approximately 0.01 microns and/or are suitable for the filtration of, for example, dissolved proteins. In one example, the microporous membrane may have a nominal pore size of approximately 0.2-1.2 microns. More typically, the nominal pore size of the membrane may be no less than approximately 0.8 microns.

PVDF is available from many different sources such as Elf Atochem of Philadelphia, Pennsylvania. In accordance with a preferred embodiment, prior to forming the membrane, the PVDF is typically dissolved in a suitable solvent. A suitable solvent for PVDF is dimethylacetamide (DMAC). In one embodiment, approximately 18-22%, by weight, of PVDF is dissolved in DMAC to provide a PVDF solution. Preferably, this PVDF solution is maintained ("cured") for approximately 18 hours at between 28-35°C and more preferably, approximately 31°C prior to forming the membrane. Of course, where other polymeric materials are used, different solvents, different curing times and temperatures may be used.

Membranes of the type described above may be made by flowcasting or extrusion. Figure 2 illustrates one method and the associated apparatus for making a membrane of the present invention. The method depicted in Fig. 2 is commonly known as a flow-casting method in which the membrane is formed continuously on a moving support surface such as a web or belt made of a suitable material. It will be understood, however, that in its broader respects, the present invention is not limited to the particular method employed in making the membrane or the presence or absence of a support surface. For example, PVDF membranes without the support, as shown in Fig. 1, may be made by applying the PVDF to a drum and thereafter peeling the membrane off the surface of the

drum. Alternatively, PVDF membranes may be made by casting a PVDF solution onto a support of the type described above, forming the membrane and then separating the membrane from the support, as described in U.S. Patent No. 4,203,848, which is incorporated by reference herein.

As shown in Fig. 2, the web or support 18 is dispensed from supply roll 22 into a V-shaped trough or chamber 24 that is filled with the cured PVDF solution 25 (described above). As support 18 passes through chamber 24, the PVDF solution is applied to the outer surfaces of the support web 18. (It will be understood that optionally, only one side of the support may be coated with the PVDF solution.) The support, with the PVDF solution applied thereon, exits the chamber through an opening at the bottom of the chamber 24. As shown in Fig.2, apparatus includes a series of rollers 36 over which the support is threaded as generally shown. Rotation of rollers 36 effects movement of the support 18 from dispenser 22 through the series of baths and drying devices, which are described in more detail below. The rate of movement of support 18 may depend on the required or desired residence times of the support (with the membrane applied thereon) within the baths and drying devices. In one embodiment, the rate of movement may be between approximately 1-5 ft/min and, more typically, approximately 3 ft/min.

The coated support 18 then passes through a first coagulation bath 26. Typically, the first coagulation bath 26 holds a liquid or solution which is a non-solvent for the polymer (e.g., PVDF) portion of the PVDF solution, but is freely miscible with the solvent portion (e.g., DMAC) of the PVDF solution. Contact with the liquid in the coagulation bath 26 coagulates the polymer

solids (PVDF) and extracts the solvent portion (i.e., DMAC) from the applied layer of PVDF, thereby forming a porous PVDF membrane on the support. This "solvent/non solvent" method of forming membranes is well known to those of skill in the art and is described in, for example, U.S. Patent No. 3,642,668, which is incorporated by reference herein.

The support 18 with the PVDF membrane on its surface is then advanced from coagulation bath 26 to one or more extraction baths 28. Typically, the extraction bath(s) will contain a liquid that extracts any residual solvent (e.g., DMAC) which was used to dissolve the polymer from the membrane. In a preferred embodiment, the liquid may be water. Depending on the type and strength of the solvent used, the membrane may undergo a series of wash steps in one or more extraction baths 28, each bath further washing and removing solvent from the membrane. For purposes of example only, three extraction baths 28 are shown in Fig. 2.

Once the solvent has been substantially extracted from the membrane, the membrane is dried. Various drying techniques may be used. For example, after the final extraction bath, the membrane may be introduced into a drying oven 40 shown in Fig. 2. Alternatively, and perhaps more preferably, the membrane may be dried by contacting the membrane sheet with one or more heated drums, which dry the membrane in a manner well understood by those of skill in the art.

In one embodiment, where drying oven 40 is used, a drying temperature of approximately 65°C or less may be sufficient to thoroughly dry the membrane. Alternatively, where a series of heated drums are used, the temperature of the first drum may be higher than the temperature of the later drums in the series to allow

substantially all of the water to be evaporated from the wet membrane. The later drums, which are set at a lower temperature (such as, but not limited to, 50°C to 60°C), ensure that the membrane is completely dry. Regardless of the drying apparatus used, excess water may also be removed from the membrane by passing the membrane between wipers 41 prior to drying, as generally depicted in Fig. 2.

After the membrane is dried, it must be further treated by coating the membrane surface with a wetting agent to make it hydrophilic. Thus, as further shown in Fig. 2, after drying, the membrane may be introduced into another bath 44 containing a hydrophilic coating solution. It will be understood that the method of coating is not limited to immersing the membrane in the coating solution, but may also include spraying or other forms of applying the wetting agent to the membrane.

In one preferred embodiment, the wetting agent is polyvinyl alcohol which has been dissolved in a solution of water and isopropyl alcohol. Polyvinyl alcohol is derived from saponified polyvinyl acetate. (Saponification refers to the process of hydrolyzing an ester). Polyvinyl alcohol is available in a variety of grades, according to the degree of saponification. In the PVDF membranes of the present invention, polyvinyl alcohol having a degree of saponification of at least about 40% may be used. Polyvinyl alcohol having a high degree of saponification, for example, greater than 80% is, however, preferred.

For immersion coating, the polyvinyl alcohol coating solution may be prepared as follows. Highly saponified polyvinyl alcohol is typically dissolved in hot water, such as water having a temperature of approximately 90°C. The dissolved polyvinyl alcohol is then further mixed

with another alcohol to provide the coating solution. In one embodiment, the coating solution includes approximately 20-80% water and 20-80% of the other alcohol, and more preferably, 40% to 60% water and 40% to 60% of the other alcohol. One particularly useful alcohol for the coating solution is isopropyl alcohol. Other simple alcohols, such as methanol, may also be suitable. In a further preferred embodiment, the coating solution may include approximately 50% water and 50% isopropyl alcohol. The polyvinyl alcohol is dissolved in the solution to provide a coating solution having approximately 0.1% to 10%, by weight, polyvinyl alcohol. Preferably, the concentration of polyvinyl alcohol in the coating solution is approximately 1-10 % and more preferably, approximately 1-2%, by weight.

In another embodiment, a less saponified polyvinyl alcohol may be used, such as polyvinyl alcohol having a degree of saponification of at least about 40% but less than approximately 80%. In this embodiment, the polyvinyl alcohol may first be dissolved in an alcohol such as isopropyl alcohol. Water may be added to achieve the water/alcohol ratios described above. Alternatively, the less saponified polyvinyl alcohol may be dissolved in a mixture of alcohol and water.

Returning now to the method of making the membrane shown in Fig. 2, the dry membrane is then immersed in the coating solution including polyvinyl alcohol. It is preferred that at the point of entry into the coating solution bath 44, the membrane not be in contact with a roller, as generally depicted in Fig. 2. Stated differently, it is preferred that the level of liquid 45 in the coating solution bath 44 be such that the membrane enters the bath 44 at a point where it is not in contact with a roller 36. This allows for better displacement of

air by the coating solution, which results in improved and/or more uniform wetting of the membrane.

Afterwards, the membrane may be further dried in another drying apparatus such as oven 48, which dries the membrane as described above in connection with the PVDF membrane prior to wetting. After drying, the membrane may be cut (to its desired width) and accumulated on take-up roll 50. The membrane may be further cut into smaller lengths or widths as necessary.

Membranes made in accordance with the present invention may have many different uses. For example, the membranes of the present invention may be used wherever a component or particle must be separated from the liquid in which it is suspended. In one specific embodiment, membranes made in accordance with the present invention may be used in a disposable processing set for separating a biological fluid such as blood into its components. For example, whole blood may be passed through the membrane to separate the whole blood into plasma, on the one hand, and concentrated blood cells (such as red cells and white cells), on the other hand. An example of a separation device or separator with which the membrane of the present invention may be used is described in more detail below. However, the separation device is only one example of possible uses for the membrane, and nothing in the description that follows should be construed as limiting the present invention to use with such a device. Indeed, membranes made in accordance with the present invention may be used in laboratory or industrial settings where the membrane is not limited to one time use, but rather may be repeatedly used.

A separator 60 that includes a PVDF membrane made in accordance with the present invention is shown in Fig.3. Separator 60 is typically part of a disposable fluid

processing used in association with a device for separating whole blood into plasma and concentrated blood cells, such as the Autopheresis-C® plasmapheresis device marketed by Baxter Healthcare Corporation. The structure and operation of the plasmapheresis device, including separator 60, are set forth in detail in U.S. Patent No. 5,194,145, incorporated by reference herein, and a detailed description will not be repeated here.

Briefly, however, as depicted in Figure 3, separator 60 includes a housing 66 defining a generally cylindrical inside surface 70. The housing includes a fluid inlet 72, a first outlet 74 and second outlet 76. A rotor 78, with a generally cylindrical outer surface, is rotatably mounted in the housing with the outer surface of the rotor spaced from the interior surface of the housing to define a small gap 82 therebetween. The membrane 10 of the present invention is mounted on the rotor, with the membrane facing gap 82 located between rotor 78 and housing 66. The membrane rests atop a series of spaced-apart support ribs 86 on the surface of the rotor. These raised support ribs support the membrane and form channels to collect filtrate passing through membrane 10.

Although the membrane is shown on the surface of the rotor in Figure 3, alternatively, the membrane may be mounted on the generally cylindrical interior surface of the housing. In that event, the surface of the housing may similarly include raised ribs to support filter membrane and to collect filtrate passing through the membrane.

In the separator 60 shown in Figure 3, fluid such as a biological suspension or blood is introduced through inlet 72 and flows down through the gap 82 between the outer surface of the rotor 78 and inner surface of the housing 66. During the passage through the gap, the

high-speed rotation of rotor generates turbulence in the form of Taylor vortices, which sweep the membrane free of clotting cells or debris. Assisted by substantial transmembrane pressure generated by flow control pumps, of the plasmapheresis device, plasma from the blood passes through membrane 10 and is collected in the channels defined between the spaced apart raised ribs. The plasma flows down through the channels into a collection manifold, and passes through first outlet 74. The remaining portion of the fluid or suspension (e.g., concentrated cells) is withdrawn from the housing through the second outlet 76.

Membranes made in accordance with the present invention, namely PVDF membranes made hydrophilic by coating such membranes with polyvinyl alcohol, are useful in the processing of blood as substantially described above in that they are biologically compatible with biological fluid, such as blood. Membranes of the present invention are particularly well-suited for sonic welding to the rotors of the type described above. As presently understood, PVDF is capable of forming alloys, during sonic welding, with the acrylic material typically used to make such rotors. This provides improved adhesion of the membrane to the rotor, resulting in improved quality and reliability of the separator and a reduced scrap rate.

Membranes of the present invention are sterilizable by radiation sterilization such as gamma radiation or electron beam radiation. An additional advantage of PVDF membranes made in accordance with the present invention, particularly when used to separate plasma from whole blood, is relatively minimal complement and platelet activation.

Complements are naturally occurring soluble proteins found in blood plasma that provide immune protection. They circulate throughout the body and become activated on exposure to an antigen and/or in the response to tissue injury. However, in some instances, the complement may become activated in the absence of activating antigen, such as by contact with the equipment used in the processing of blood. Since these complements are essential to the immune response in humans, it is desirable that complement activation during blood processing be kept to a minimum.

Platelets are essential in the repair of injured body tissue in that they help form clots and prevent excess bleeding. However, platelets may also become activated by contact with the equipment used in the processing of blood, including the membranes used for separating the blood components. Accordingly, it is also desirable that platelet activation be kept to a minimum.

Using a blood separator of the type substantially described above (the Plasmacell-C® separation chamber used with the Autopheresis C®, both available from Baxter Healthcare Corporation of Deerfield, IL), whole blood was collected from donors in two different anticoagulants (sodium citrate and ACD-A). The blood was separated into plasma and concentrated cells. Samples of the donor's blood were taken before and after the separation procedure. Samples of the collected plasma and concentrated cells (CCC) were also taken. The samples were assayed for complement activation and platelet activation.

The results of the assays are set forth below in the following Tables 1 and 2.

TABLE 1

MEAN COMPLEMENT C3a AND C5a RESULTS

MEASUREMENT	DONOR PRE- (mean ± SD)	CCC (mean ± SD)	PLASMA (mean ± SD)	DONOR POST (mean ± SD)
C3a (ng/mL)				
NaCitrate	53.88±27.53	144.92±38.97	1101.06±297.22	63.72±20.75
ACD-A	55.28±37.55	295.89±264.55	1650.02±671.62	139.95±162.56
C5a(ng/mL)				
NaCitrate	10.65±3.10	10.37±3.63	23.26±5.23	9.81±4.56
ACD-A	9.60±1.96	13.67±5.05	21.91±8.71	11.98±3.16

N=10

As shown in Table 1, although the processing of blood, as described above, did result in some complement activation, the levels of complement activation were generally lower than levels previously observed with other membranes and/or materials.

The results of the platelet activation assays are set forth below in Table 2. The presence of CD62 on the platelet surface and the presence of β-thromboglobulin and Platelet Factor 4 in plasma are evidence of platelet activation.

TABLE 2

PLATELET ACTIVATION TEST RESULTS

MEASUREMENT	DONOR PRE- (mean ± SD)	CCC (mean ± SD)	PLASMA (mean ± SD)	DONOR POST (mean ± SD)
CD62%				
NaCitrate	6.09±5.05	27.38±19.26	NT	7.97±6.14
ACD-A	3.88±2.08	8.83±4.00	NT	3.82±1.36
β-tg (IU/ml)				
NaCitrate	792±646	2802±2418	207±137	612±323
ACD-A	723±605	2861±2109	167±112	592±416
PF4 (IU/ml)				
NaCitrate	340±361	1382±748	49±45	210±136
ACD-A	373±314	1408±902	73±66	306±242

As shown in Table 2, although processing of blood using the membrane of the present invention did result in some platelet activation, the levels of platelet activation in the plasma component were comparable to the preprocedure and postprocedure levels, suggesting that there was no additional platelet activation caused by the apparatus and/or procedure.

Although the membranes of the present invention have been described above in the context of and as part of a one time use disposable processing set for blood and blood components, membranes of the present invention may also be used in other settings where reusability of the membranes is desired. For example, it has been observed that membranes made in accordance with the present invention remain hydrophilic even after repeated use. Stated differently, membranes of the present invention are capable of being "rewet" after such use, and after drying. As used herein, "rewet" or "rewettable" refers to the ability of a membrane that has been previously wet and dried to substantially absorb a contacting aqueous liquid (i.e., without the presence of any dry spots) in less than about 1 minute.

Moreover, the membranes of the present invention remain hydrophilic even though they are "non-crosslinked." Although, it is possible that a small amount of cross-linking may occur during manufacture of the membrane, it will be understood that such minimal and incidental cross-linking is within the meaning of "non-crosslinked", as that term is used herein.

Membranes made in accordance with the present invention were wet, dried and rewet with an aqueous liquid to demonstrate the rewetability of such membranes. The tests and results thereof are described below.

EXAMPLE 1

PVDF membranes treated with 1% PVOH in the manner set forth above were placed into a Gelman filtration funnel and approximately 600 ml of room temperature water was passed through the membrane. The membrane was then dried at 70°C for approximately 5 minutes and then contacted with a 0.9% saline solution. It was observed that the membrane rewet immediately. The same membrane was then again placed into a funnel and approximately 800 ml of water at 40°C was filtered through the membrane. The membrane was dried and after drying, contacted with 0.9% saline. It was observed that the membrane rewet immediately.

EXAMPLE 2

Samples of membranes made as substantially described above were placed in beakers filled with approximately 800 ml of water. The beakers were placed on a hot plate and the water was heated to boiling. A magnetic stir bar along with the four membrane samples were placed into the water. After boiling for 1 ½ hours, the membranes were allowed to dry. After drying, room temperature water was passed through the membrane. The membranes were then dried again at 50°C for approximately one hour and then contacted again with room temperature water. It was observed that the boiled, dried membranes rewet after less than approximately five seconds.

Accordingly, even after boiling in hot water and drying such membranes, the membranes retain their hydrophilic properties and were reusable as membranes. This is in contrast to PVDF membranes that have been prepared by the same process described above, but treated with other known wetting agents, such as polyethyleneglycol (PEG). PVDF membranes rendered hydrophilic with a 5% PEG coating solution (dissolved in

water and isopropyl alcohol) wet initially, but did not rewet after drying.

The present invention has been described in accordance with its preferred embodiments. However, it will be appreciated that various modifications to the membranes and the methods of making these membranes are possible without departing from the scope of the present invention which is set forth in the appended claims set forth below.

THAT WHICH IS CLAIMED:

1. A microporous membrane comprising:

a porous layer of polyvinylidene difluoride;

a polyvinyl alcohol coating on said porous layer of polyvinylidene difluoride sufficient to render said polyvinylidene difluoride hydrophilic;

wherein said membrane is rewettable by an aqueous liquid after drying and is non-cross-linked and is not contacted with a strong alkali solution.

2. The membrane of Claim 1 wherein said membrane is rewettable after contact with an aqueous liquid having a temperature of at least approximately 40°C.

3. The membrane of Claim 1 wherein said membrane is rewettable after contact with an aqueous liquid having a temperature of approximately 100°C.

4. The membrane of Claim 1 wherein said aqueous liquid is water.

5. The membrane of Claim 1 wherein said polyvinyl alcohol coating is made from a solution of 1-2%, by weight, of polyvinyl alcohol dissolved in a mixture of water and an alcohol.

6. The membrane of Claim 1 wherein said polyvinyl alcohol is derived from polyvinyl acetate having a degree of saponification of at least about 40%.

7. The membrane of Claim 6 wherein said degree of saponification is approximately 80-100%.

8. The membrane of Claim 5 wherein said alcohol in which said polyvinyl alcohol is dissolved comprises isopropyl alcohol.

9. The membrane of Claim 8 wherein said coating solution comprises, by weight, between approximately 20-80% water and approximately 20-80% isopropyl alcohol.

10. The membrane of Claim 1 wherein the nominal pore size of said membrane is no less than approximately 0.8 μm.

11. The membrane of Claim 1 wherein said layer of polyvinylidene difluoride is supported by a layer of a porous material.

12. The membrane of claim 11 wherein said porous material comprises a polyester mesh.

13. A method for making a microporous, non-cross linked, re-wettable, hydrophilic polyvinylidene difluoride (PVDF) membrane comprising:

a) providing a porous, dry, hydrophobic PVDF membrane;

b) contacting said membrane with a coating solution of 0.1-10%, by weight, of polyvinyl alcohol dissolved in a solution of water and an alcohol.

14. The method of Claim 13 comprising providing said coating solution by dissolving polyvinyl alcohol in water and thereafter adding an alcohol to said polyvinyl alcohol dissolved in water.

15. The method of Claim 13 comprising dissolving said polyvinyl alcohol in a solution comprising approximately 20-80% water and approximately 20-80% isopropyl alcohol.

16. The method of Claim 13 wherein said coating solution comprises approximately 1%, by weight, of polyvinyl alcohol.

17. The method of Claim 13 comprising providing polyvinyl alcohol having a degree of saponification of at least 80% and dissolving said polyvinyl alcohol in an aqueous solution.

18. The method of Claim 17 wherein the temperature of said aqueous solution is approximately 90°C.

19. The method of Claim 13 wherein said contacting is carried out by passing said membrane through a bath of said coating solution.

20. A microporous membrane made in accordance with the process of Claim 13.

21. Apparatus for separating a biological fluid into two or more components comprising:

a housing comprising an interior wall defining a fluid chamber and a fluid inlet and at least one fluid outlet, said inlet and outlet communicating with said chamber;

a rotor disposed within said chamber;

a microporous membrane disposed on either one of said interior wall or said rotor, said membrane comprising a porous layer of polyvinylidene difluoride and a polyvinyl alcohol coating thereon sufficient to render said polyvinylidene fluoride layer hydrophilic.

22. Apparatus of Claim 21 wherein said membrane is sonic welded to said rotor.

FIG. 1

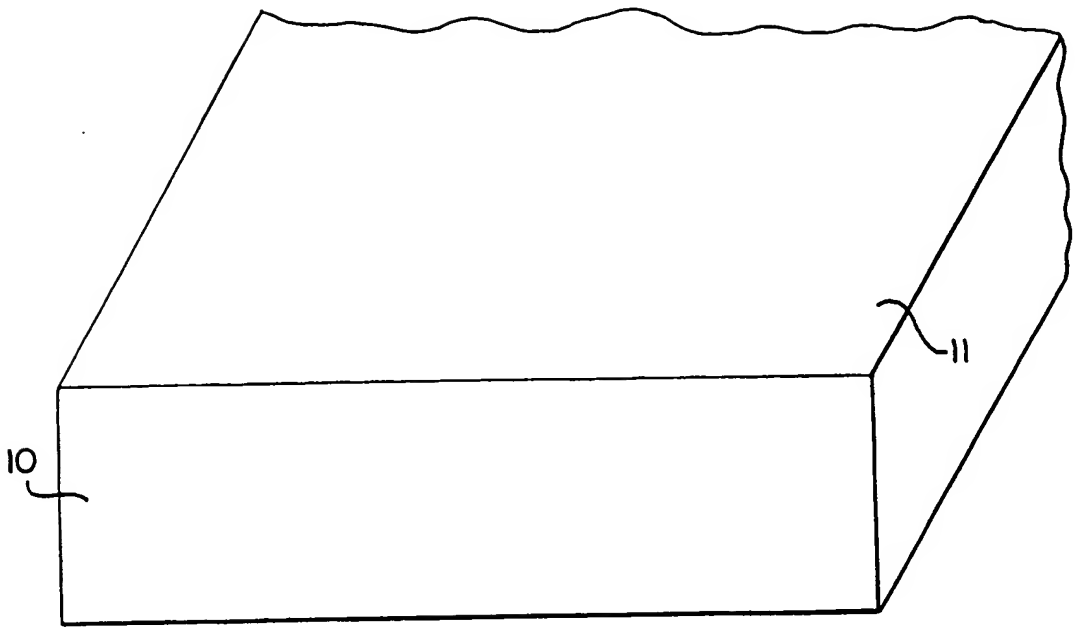


FIG. 1A

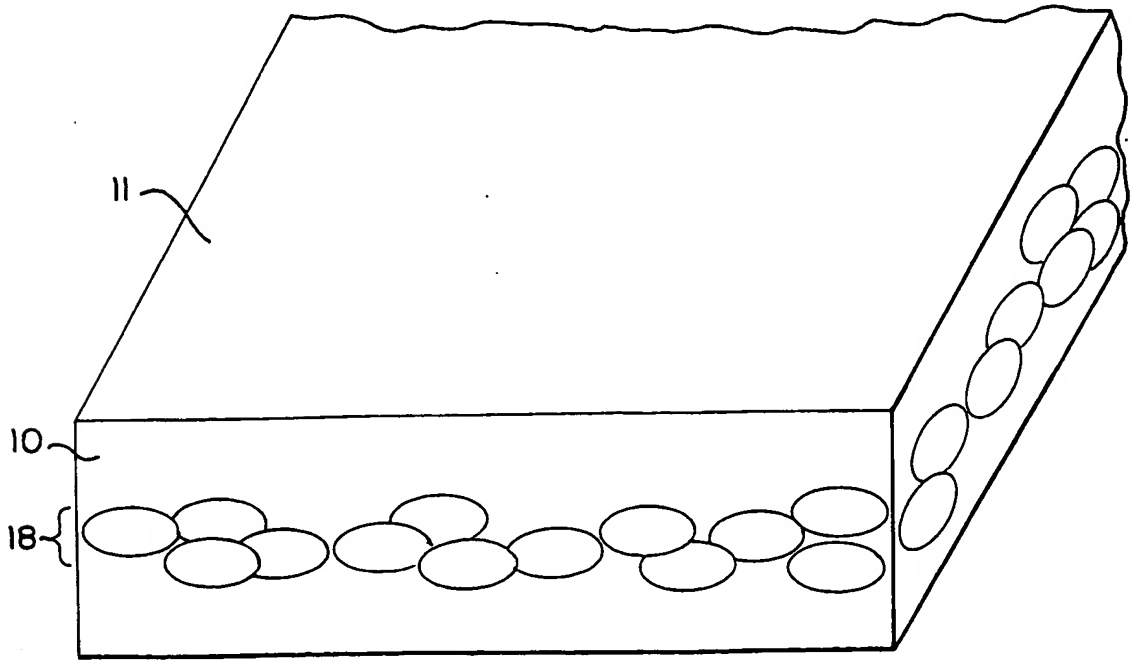


FIG. 2

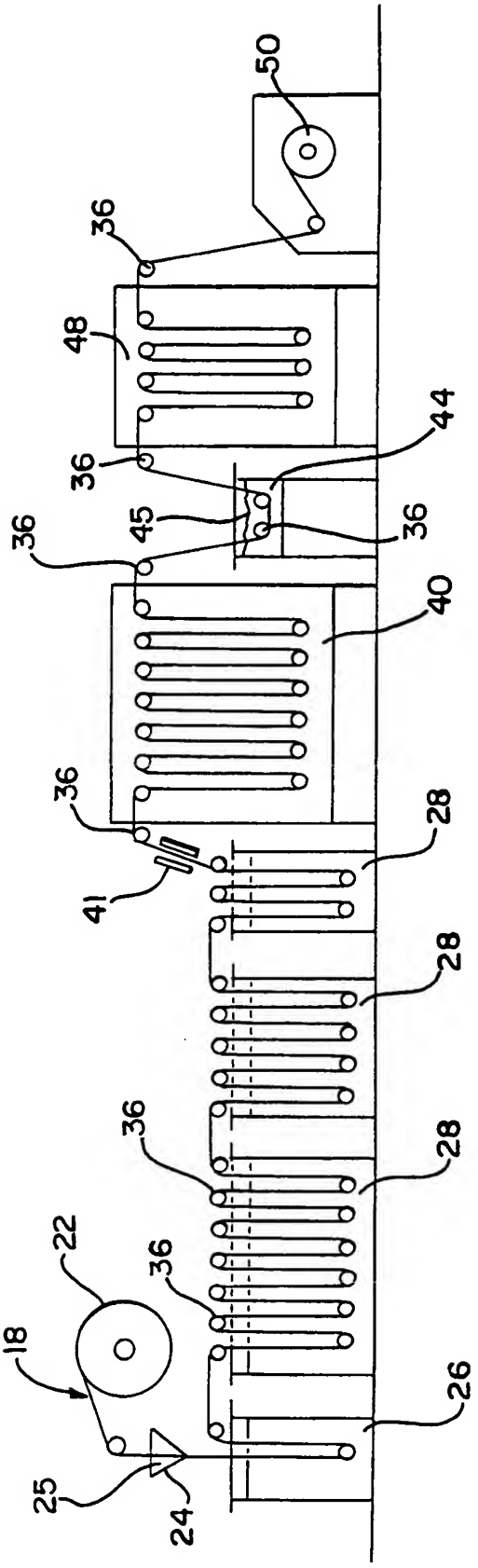
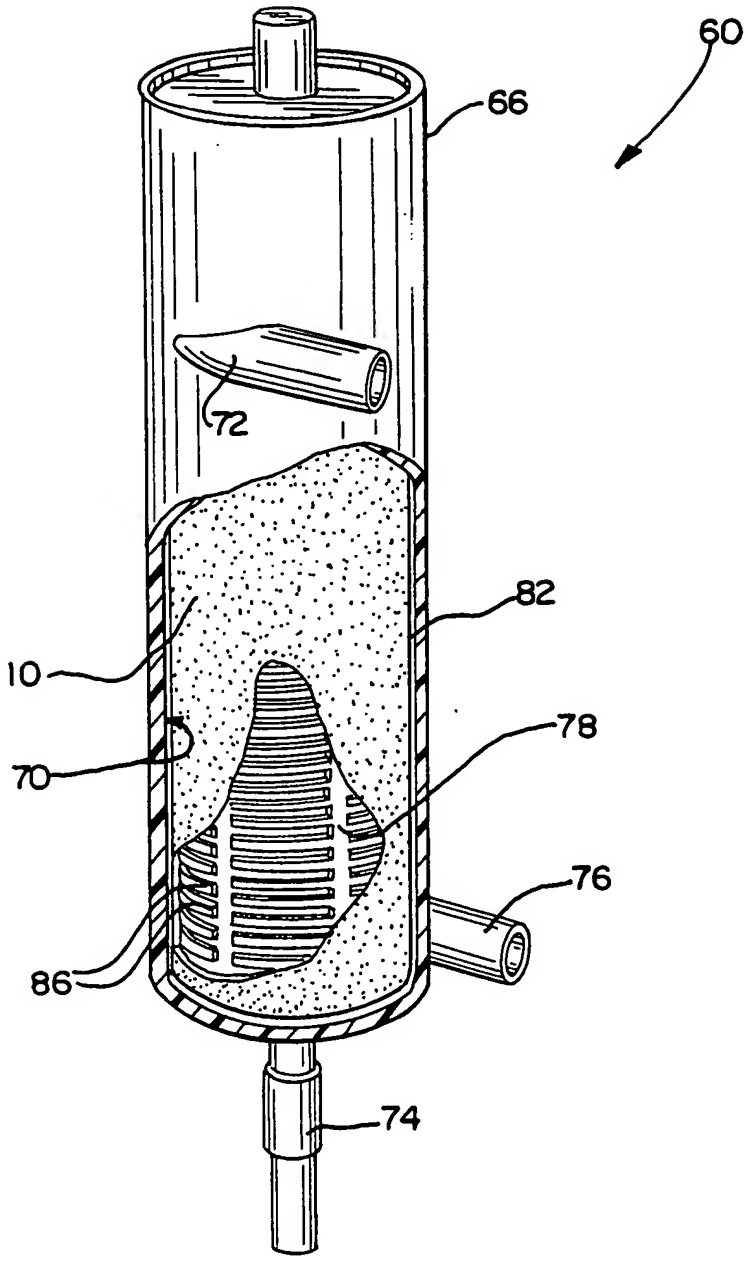


FIG. 3



INTERNATIONAL SEARCH REPORT

International application No.
PCT/U[redacted]6446

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :B01D 71/28
US CL :210/500.27, 490, 500.42; 264/41, 48,49

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 210/500.27, 490, 500.42; 264/41, 48,49

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ---- Y	US 5,091,086 A (STENGAARD) 25 February 1992, entire disclosure	1-5 ---- 6-22
Y	US 4,776,959 A (KASAI et al) 11 October 1988, entire disclosure.	1-6, 8-16, 19-22
Y	US 4,113,912 A (OKITA) 12 September 1978, entire disclosure.	1-17, 19-22
Y	DT 3220570 A (GFT ING INDANLAGENB) 01 December 1983, abstract.	1-20
Y	JP 2245227 A (FUJI PHOTO FILM KK) 01 October 1990, abstract.	1-20
Y	JP 227706 A (NITTO ELECTRIC IND KK) 02 December 1987, abstract.	1-20

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 01 AUGUST 2000	Date of mailing of the international search report 24 AUG 2000
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Form PCT/ISA/210 (second sheet) (July 1998)*